No. 22A902

IN THE SUPREME COURT OF THE UNITED STATES

U.S. FOOD AND DRUG ADMINISTRATION, ET AL., APPLICANTS

v.

ALLIANCE FOR HIPPOCRATIC MEDICINE, ET AL.

REPLY IN SUPPORT OF APPLICATION FOR A STAY

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Absent a stay, the lower courts' unprecedented nationwide orders would scramble the regulatory regime governing a drug that FDA determined was safe and effective under the approved conditions and that has been used by more than five million American women over the last two decades. Every extant package of Mifeprex would instantly become misbranded and could not be lawfully introduced into interstate commerce. The generic version of the drug, which accounts for most of the market, would cease to be approved altogether. And before Danco could resume introduction of the drug into interstate commerce, FDA would be forced to change the drug's labeling and other regulatory materials -- including by reinstating an obsolete dosing regimen that provides for women to take more of the drug than necessary. Respondents do not even begin to justify that extraordinarily disruptive result.

Respondents do not seriously defend the Fifth Circuit's "statistical" approach to associational standing, Appl. App. 17a, 19a, or the court's failure to ask whether respondents' purported injuries are traceable to the specific FDA actions at issue. But respondents' primary standing theory reduces to the same thing: They assert that because some of their members allegedly have treated patients for adverse events associated with mifepristone in the past, some of their (unidentified) members are likely to be asked to do so again at some (unidentified) point in the future. Respondents still have not cited any prior decision, from any court, endorsing such a theory. With good reason: To support a claim for prospective relief, this Court's precedents demand a showing that a specific, identified plaintiff (or association member) faces an imminent, concrete injury traceable to the defendant's challenged action. Respondents have not even attempted to make that showing here.

In addition, respondents' standing argument -- indeed, their entire submission to this Court -- rests on a wholly misleading portrayal of mifepristone's well-documented safety record. Respondents ignore the mountain of evidence and experience validating the judgment of FDA and other regulators around the world that mifepristone is extremely safe when used in accordance with its approved conditions of use. In lieu of scientific evidence, respondents point primarily to their own declarations, which are anecdotal, conclusory, or both. And respondents mischaracterize

the statistics on which they rely -- persistently conflating, for example, the need for non-emergency follow-up care with more serious adverse events, which are extraordinarily rare.

Respondents' arguments on the merits fare no better. They do not deny that no prior court has purported to invalidate FDA's regulatory regime for a drug based on judicial second-guessing of FDA's safety determinations. They offer no principle or precedent to support the Fifth Circuit's insistence that a drug's approved conditions of use exactly replicate a prior study -- a requirement the pharmaceutical industry has denounced as unworkable and destabilizing. And although respondents try to supplement the Fifth Circuit's cursory reasoning by quibbling with the details of a few of the studies on which FDA relied, they ignore dozens of others.

Finally, respondents' submission further confirms that the balance of the equities overwhelmingly favors a stay. Respondents cannot show that they will suffer any harm from maintaining the longstanding status quo pending an expedited appeal in the Fifth Circuit. And respondents have no answer at all to the profoundly disruptive effects of the lower courts' orders. Instead, respondents pretend that those effects will not occur. Like the Fifth Circuit, they deeply misunderstand the regulatory framework and presume that mifepristone's pre-2016 conditions can simply and automatically "snap back," allowing continued -- although substantially more restricted -- access to the drug. Appl. App. 113a. But as FDA's Principal Deputy Commissioner explained in a detailed

declaration, "[t]he reality is far more disruptive," and effectuating the changes required by the lower courts' orders would require extensive actions by FDA, ibid. -- some of which risk violating a separate preliminary injunction. The lower courts' orders would thus create "significant chaos for patients, prescribers, and the health care delivery system." Id. at 116a. Respondents do not even acknowledge that reality. Nor do they justify the harm of denying women lawful access to a drug under conditions FDA determined are safe and effective and instead requiring them to undergo invasive surgical procedures. This Court should issue a stay to preserve the status quo and avoid those disruptive results.

I. THIS COURT WOULD LIKELY GRANT REVIEW AND REVERSE IF THE FIFTH CIRCUIT AFFIRMED THE DISTRICT COURT'S ORDER

This Court would likely grant review if the Fifth Circuit affirmed the district court's sweeping and unprecedented order. Appl. 18-19. Respondents object (Opp. 13-14) that "there is no circuit split." But even in the absence of a square circuit conflict, this Court has not hesitated to grant stays -- and, when necessary, certiorari -- in response to lower court orders blocking important national policies. See, e.g., FDA v. American Coll. of Obstetricians & Gynecologists, 141 S. Ct. 578 (2021); Wolf v. Innovation Law Lab, 141 S. Ct. 617 (2020); DHS v. New York, 140 S. Ct. 599 (2020). So too here. And if the Court granted review, it would likely reverse. Indeed, respondents' opposition only underscores the weakness of the lower courts' analysis.

A. Respondents Lack Standing

The government's application explained that the Fifth Circuit ignored this Court's precedents by holding that respondents have associational standing because it is statistically likely that some of their unidentified members will be asked to treat adverse events associated with mifepristone. Appl. 20-28. Respondents fail to rehabilitate that novel theory, and their two alternative theories are likewise meritless.

1. Respondents Do Not Have Associational Standing

Respondents renew their assertion (Opp. 15-22) that their allegations that some of their members have treated complications from mifepristone in the past suffice to give them Article III standing to challenge FDA's 2016, 2021, and 2023 actions changing the drug's conditions of use. That argument ignores basic Article III principles and rests on factual assertions that are demonstrably at odds with the record.

a. As respondents are forced to acknowledge (Opp. 28), past harm is insufficient to establish standing to seek prospective relief. In Summers v. Earth Island Institute, 555 U.S. 488 (2009), an environmental association challenged regulations facilitating timber-salvage projects. At least one of the association's members had been harmed by a past project. Id. at 495. This Court held, however, that such past harm "does not suffice" to show standing "because it relates to past injury rather than imminent future injury that is sought to be enjoined." Id. at 495-496. Instead,

this Court's precedents require a plaintiff seeking prospective relief to establish a "threatened injury" that is "certainly impending." Clapper v. Amnesty Int'l USA, 568 U.S. 398, 409 (2013) (citation omitted). And the Court has emphasized that "'allegations of possible future injury' are not sufficient." Ibid. (brackets and citation omitted).

The Fifth Circuit tried to fill that gap with a "statistical" approach, reasoning that even if neither the named plaintiffs nor any other identified member of the respondent associations has standing, respondents may nonetheless sue because (in the court's view) it is inevitable that at least "one doctor among the thousands of members in these associations faces an injury." Appl. App. 17a-18a. Respondents do not defend that "statistical-probability-of-injury-to-a-member theory" (Opp. 29), which is equivalent to the theory Summers dismissed as "mak[ing] a mockery" of Article III. 555 U.S. at 498. Associational standing is not a device for manufacturing standing by aggregating speculative injuries to individual members when those injuries would not themselves satisfy Article III. Instead, this Court has emphasized that Article III requires an organization to "make specific allegations establishing that at least one identified member" will suffer harm. Id. at 498 (emphasis added). And "[t]his requirement of naming the affected members has never been dispensed with in light of statistical probabilities." Id. at 498-499.

b. Respondents have not met that requirement. They principally contend (Opp. 15-17) that one or more unidentified doctors will be required, against their conscience, to complete an abortion for a patient who has taken mifepristone. But respondents entirely ignore the federal conscience protections that would guard against that result, including the Church Amendments, 42 U.S.C. 300a-7 et. seq., the Weldon Amendment, Consolidated Appropriations Act, 2022, Pub. L. No. 117-103, Div. H., Tit. V, §§ 506–507, and Section 245 of the Public Health Service Act, 42 U.S.C. 238n. Respondents' feared injury thus depends on a highly speculative string of events: that a woman will obtain mifepristone from another provider; that she will suffer an extremely rare adverse event; that such event will require emergency treatment; that rather than returning to her provider or another individual the provider previously identified, she will present at an emergency room where one of the respondents or member doctors is working at the time; that the adverse event will require an emergency abortion; and that, despite federal conscience protections and the likely presence of other, non-objecting doctors, the objecting doctor will be required to provide the abortion. Respondents cite no prior decision finding standing based on such an attenuated and speculative theory.

Respondents assert (Opp. 29) that the lower courts identified specific doctors who faced such imminent harm. But respondents cite no such finding, and none exists. In fact, over the nearly

23 years mifepristone has been on the market -- and across the more than 5 million Americans who have used it to end a pregnancy -- respondents purport to identify only "three doctors" among their thousands of members who stated "that they were faced with emergency situations and forced to perform and participate in elective abortions because women were suffering life-threatening conditions from mifepristone." Opp. 28 (citing Resps. C.A. App. 5-7, 16-19, 111); see id. at 16 (citing the same three declarations). Even taken at face value, three examples from over 20 years of experience would not suggest that any particular doctor faces an imminent threat of such an occurrence.

In fact, respondents' description of their alleged injuries overstates their evidence. Their first declaration recounts the experience of the declarant's unidentified partner. Resps. C.A. App. 6. The other two declarations recount (1) a procedure to treat heavy bleeding and uterine infection; and (2) a procedure to resolve pregnancy tissue remaining in the uterus. Id. at 16, 111. To the extent the declarants objected to performing such procedures, neither explains why they did not seek to invoke federal conscience protections. Respondents' allegations thus do not come close to demonstrating that an identifiable respondent or member of a respondent organization faces an imminent risk of being re-

quired to complete an abortion because of FDA's challenged actions.[1]

Respondents' other allegations are also flawed. They assert (Opp. 18-20) that treating mifepristone patients has caused them "stress" and required them to divert resources from other patients. But even assuming that being presented with such a patient would constitute an Article III injury to a legally protected interest, it is speculative that any particular doctor will experience such an effect in the future. And respondents' allegations simply underscore how unbounded their standing theory is. Surely some emergency room doctors find it stressful to treat gun-shot victims, drunk drivers, or individuals experiencing an opioid overdose, and they sometimes must divert resources to care for such patients -- that is the nature of triaging patients in an emergency room. If respondents' allegations permit them to challenge FDA's actions with respect to mifepristone, other doctors would likewise have standing to sue a multitude of manufacturers and regulators. Respondents' assertion (Opp. 15, 21-22) that FDA's regulatory actions with respect to a drug they do not prescribe causes them to

[1] Repeating the Fifth Circuit's error, respondents suggest (Opp. 27) that their claims of harm are "sufficiently imminent" because mifepristone's Patient Agreement Form notes that when medication abortion is unsuccessful, patients should speak with their providers about other options, including surgical abortion. But the Agreement advises patients to speak with their providers -- not with respondents. As FDA has explained (Appl. 24-26), that advice does nothing to support respondents' claim that such women will require an emergency surgical abortion from respondents, their members, or anyone at all.

face increased exposure to third parties' malpractice allegations and higher insurance costs is similarly flawed. Respondents cite no documented instance of such effects (just their own conclusory declarations), nor any case supporting that speculative, attenuated, and limitless theory of standing.[2]

c. Respondents also fail to overcome the Fifth Circuit's other fundamental error: The Fifth Circuit dispensed standing "in gross," TransUnion v. Ramirez, 141 S. Ct. 2190, 2208 (2021), reasoning that respondents are injured by the availability of mifepristone in general rather than the specific FDA actions that respondents challenge in their timely claims. Appl. 26-27. Neither the Fifth Circuit nor the district court even purported to find that respondents' alleged injuries are "fairly traceable" to FDA's post-approval actions, rather than the general availability of mifepristone. Friends of the Earth, Inc. v. Laidlaw Environmental Servs. (TOC), Inc., 528 U.S. 167, 180 (2000). Nor did the lower courts find that relief targeted to FDA's post-approval actions would alleviate those injuries.

In an attempt to cure that defect, respondents assert (Opp. 22-26) that the 2016 changes have increased the number of women

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[2] Respondents at times suggest that they have demonstrated standing based on a "substantial risk that the harm will occur." Opp. 28 (quoting Susan B. Anthony List v. Driehaus, 573 U.S. 149, 158 (2014)). "But to the extent that the 'substantial risk' standard is relevant and is distinct from the 'clearly impending' requirement," it does not permit plaintiffs to demonstrate standing based on an "attenuated chain of inferences." Clapper, 568 U.S. at 414 n.5.

who take mifepristone and then require treatment at an emergency room. But even though it has been seven years since the 2016 changes, respondents do not cite any scientific or empirical evidence of such an increase. Instead, they rely almost entirely on conclusory statements in their own complaint and declarations. See, e.g., Resps. C.A. App. 4, 25, 32, 90, 105-106, 113, 253, 265. Those bare assertions do not suffice.[3]

2. Respondents' Alternative Theories Lack Merit

Respondents briefly attempt to revive (Opp. 30-33) two additional standing theories that the Fifth Circuit declined to adopt. Neither has merit.

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[3] Respondents suggest (e.g., Opp. 24, 26) that elimination of the in-person dispensing requirement poses a particular risk to women experiencing undiagnosed ectopic pregnancies. Respondents cite no evidence suggesting that mifepristone exacerbates ectopic pregnancy; rather, it simply is not effective in resolving that condition. As FDA recognized, there are myriad ways to diagnose ectopic pregnancy, not all of which require an in-person physical exam. See, e.g., C.A. Add. 821-822. And like the rest of their alleged injuries, plaintiffs' asserted harms related to ectopic pregnancy rest on a series of speculative events: that a woman with an ectopic pregnancy will be prescribed mifepristone; that her ectopic pregnancy will rupture before she confirms with her provider that she is no longer pregnant; that she will mistake the symptoms associated with an ectopic rupture for the normal medication abortion process; that she will thus delay seeking treatment, thereby experiencing greater complications than she would have without having taken mifepristone; and that (unidentified) respondents will be forced to treat such complications -- despite the fact that ectopic pregnancy occurs in just 0.005 percent of women who use mifepristone, C.A. Add. 418; see Isabel Besnar, et al., Discovery of an Ectopic Pregnancy after Attempted Self-Managed Abortion, 388 New Eng. J. Med. 278-279 (2023), https://perma.cc/QES7-9SKB (source on which respondents rely stating that "[e]arly data do not suggest an increased incidence of ectopic pregnancy detected after abortion with the use of no-touch protocols").

a. Respondents assert that they have organizational standing because they have "diverted valuable resources away from [their] advocacy and educational efforts" in order to oppose FDA's actions related to mifepristone. Opp. 31 (citation omitted). But surely the environmental association in Summers could have said much the same thing. Respondents again offer no limiting principle for their theory, which would entitle any organization to manufacture standing to challenge any government action merely by expending resources in opposing it. This Court has made clear that parties who do not face some actual, concrete injury "cannot manufacture standing merely by inflicting harm on themselves." Clapper, 568 U.S. at 416.[4]

b. Respondents also contend (Opp. 32-33) that they have third-party standing to assert claims on behalf of unidentified women who might be prescribed mifepristone by other providers and then seek care from respondents. Cf. Appl. App. 10a-11a n.4 (declining to address this issue). That theory is doubly wrong.

First, it rests on a basic misunderstanding of third-party standing doctrine. That doctrine is not a substitute for the "irreducible constitutional minimum of standing," which requires "the plaintiff" -- not a third party -- to have "suffered an

[4] The Fifth Circuit adopted a narrower theory of organizational injury based on respondents' alleged loss of adverse-event information. Appl. App. 22a. But respondents do not defend that holding, which in any event would give them standing to challenge only FDA's changes to mifepristone's adverse-event reporting requirements. Appl. 27-28.

'injury in fact.'" Lujan v. Defenders of Wildlife, 504 U.S. 555, 560 (1992). Instead, third-party standing is an exception to the "prudential" rule that even a plaintiff with Article III standing ordinarily cannot "rest his claim to relief on the legal rights or interests of third parties." Kowalski v. Tessmer, 543 U.S. 125, 128-129 (2004) (citation omitted). This Court has held, for example, that doctors directly regulated by restrictions on abortion may challenge those restrictions by asserting their patients' rights. See June Med. Servs. L.L.C. v. Russo, 140 S. Ct. 2103, 2117-2120 (2020), overruled on other grounds, Dobbs v. Jackson Women's Health Org., 142 S. Ct. 2228 (2022). This case is entirely different. Unlike the doctors in June Medical, respondents do not merely seek to assert the legal rights of their hypothetical future patients; instead, they seek to use alleged harms to those third parties to cure their own lack of injury in fact. Respondents cite no precedent endorsing such an end-run around Article III's "irreducible constitutional minimum." Lujan, 504 U.S. at 560.

Second, respondents would not satisfy the requirements for third-party standing in any event. They do not have "a 'close' relationship" with the "as yet unascertained" patients they purport to represent. Kowalski, 543 U.S. at 130-131 (citation omitted). And they cannot plausibly claim to represent those patients because their interests are diametrically opposed: Respondents seek to block access to mifepristone, but the hypothetical patients they posit are, by definition, women who choose to use the drug.

B. FDA's Actions Were Lawful

Even if respondents could establish Article III standing, their claims would fail on the merits.

1. FDA's Actions Were Not Arbitrary Or Capricious

The Fifth Circuit held that respondents are likely to succeed on the merits of their claim that FDA acted arbitrarily and capriciously in approving changes to mifepristone's conditions of use in 2016, in modifying adverse event reporting requirements at the same time, and in eliminating the in-person dispensing requirement in 2021 and 2023. But the Fifth Circuit's cursory merits analysis failed to grapple with FDA's careful evaluation of the record before the agency, which showed that serious adverse events from mifepristone are "exceedingly rare" under the approved conditions. C.A. Add. 707; see Appl. 28-37.

Respondents neither rehabilitate the Fifth Circuit's analysis nor provide any other justification for overriding FDA's considered scientific judgment. The arbitrary and capricious standard is "deferential," and a reviewing court's only role to ensure "that the agency has acted within a zone of reasonableness" and "has reasonably considered the relevant issues and reasonably explained the decision." FCC v. Prometheus Radio Proj., 141 S. Ct. 1150, 1158 (2021). FDA more than discharged that obligation here.

a. In 2016, FDA increased mifepristone's gestational age from seven to ten weeks, reduced the number of required clinical visits from three to one, and allowed non-physician health care

providers to prescribe mifepristone. In finding that each of those changes would not undermine mifepristone's safety or effectiveness, FDA relied on multiple studies -- dozens, in total -- involving tens of thousands of women. Appl. 29-30.

The Fifth Circuit's sole basis for deeming those changes arbitrary and capricious was its assertion that FDA failed to consider the changes "as a whole" because it did not have a study combining all three of them. Appl. App. 35a. A wide range of industry participants have emphasized that it would be "rigid, unworkable, and entirely unnecessary" to require FDA to identify a study precisely matching a drug's approved conditions of use. Amicus Br. of Pharmaceutical Cos. 14; see Appl. 31-33. Respondents do not even attempt to ground the Fifth Circuit's approach in the FDCA or square it with traditional principles of administrative law. Nor, for that matter, do respondents offer any reason to assume that three changes that proved to be entirely safe in isolation would become dangerous in combination -- much less any evidence to that effect. And respondents wholly ignore that the Fifth Circuit was wrong on the facts in any event. They repeatedly assert that FDA "looked at 'zero' studies" involving the three approved changes together (Opp. 38), but ignore that Winikoff 2012, for example, combined all three: gestational ages greater than seven weeks, one clinical visit at the outset, and care provided by non-physicians.

Against all this, respondents criticize (Opp. 34-35) various features of a handful of the dozens of studies on which FDA relied. But neither the district court nor the Fifth Circuit endorsed those objections, many of which respondents do not even purport to have presented to FDA itself. And the deferential arbitrary and capricious standard does not give litigants or the courts a license to second-guess "highly technical determination[s] committed to [an agency's] expertise and policy discretion." Am. Radio Relay League, Inc. v. FCC, 524 F.3d 227, 248 (D.C. Cir. 2008) (Kavanaugh, J., concurring in part). This Court has acknowledged that agencies sometimes operate without "perfect empirical or statistical data," and that an agency must be free to make "a reasonable predictive judgment based on the evidence it had." Prometheus Radio, 141 S. Ct. at 1160. That is what FDA did with respect to mifepristone. Appl. 29-34.

In any event, respondents' specific objections lack merit. For example, respondents object (Opp. 35) that the Winikoff 2012 and Smith[5] studies -- both of which tested conditions nearly identical to those ultimately approved in 2016 -- were primarily designed to study "efficacy," not safety. But both studies concluded that mifepristone was safe as well as effective. See D. Ct. Doc. 8, at 658-659 (Winikoff 2012) ("occurrence of major adverse events

[5] Smith et al., Safety, efficacy and acceptability of outpatient mifepristone-misoprostol medical abortion through 70 days since last menstrual period in public sector facilities in Mexico City, 44 Reproductive Health Matters (2015), Supplement 75-82.

in this study was very infrequent"); Smith at 79 (discussing "rates of efficacy and acceptability").[6] And FDA's decision about the safety of the 2016 changes also incorporated additional studies -- not challenged by respondents -- that "extensively" studied "[t]he proposed dosing regimen" and found that "[s]erious adverse events * * * are rarely reported." C.A. Add. 787.

Respondents similarly object (Opp. 34) that FDA's decision extending mifepristone's gestational limit from seven to ten weeks was "based on a study involving initial ultrasound exams and follow-up exams," even though FDA did not impose those requirements in the approved 2016 conditions of use. To the extent respondents are suggesting that FDA considered only "a" study, they seriously misrepresent the record. FDA's analysis of the gestational age issue incorporated nearly a dozen studies covering thousands of patients. See C.A. Add. 695, 697. Respondents are likewise mistaken to the extent they suggest FDA failed to consider the necessity of ultrasound and clinical follow-up. FDA addressed both points at length in responding to respondents' citizen petitions. See C.A. Add. 820-822, 831, 849-855. These aspects of the record, which respondents and the lower courts simply ignore, conclusively demonstrate that FDA did not "fail[] to respond meaningfully" to

[6] Respondents also attempt to discount the Winikoff 2012 and Smith studies because some patients failed to follow up with investigators and thus were dropped from the studies. But that is a common occurrence in studies. FDA specifically acknowledged this feature of the studies but reasonably found their data relevant. See C.A. Add. 695 (listing percentage of patients "Lost to Follow up").

respondents' objections. Opp. 35 (quoting In re NTE Conn., LLC, 26 F.4th 980, 989 (D.C. Cir. 2022)).

b. Respondents assert (Opp. 36) that FDA acted arbitrarily by modifying mifepristone's reporting requirements in 2016. But FDA made those changes after fifteen years of adverse event data that showed "known risks occurring rarely." C.A. Add. 856; see Appl. 35-37. By that point, mifepristone's "well-characterized safety profile" was firmly established. C.A. Add. 856. And while FDA changed the reporting requirements for certified prescribers to report certain adverse events, it did not eliminate them. FDA still requires prescribers to report any deaths, permits prescribers and patients to voluntarily report other adverse events, and requires the drug's sponsors to report all adverse events of which they are aware, including non-fatal ones. See Appl. 35-37. Contrary to respondents' repeated insinuations, the existing reporting requirements for mifepristone are neither lax nor meaningless. Indeed, because FDA preserved the requirement to report deaths, mifepristone "remains subject to a more rigorous adverse event reporting regime than the vast majority of other drugs on the market." Amicus Br. for Food and Drug Law Scholars 15 (comparing requirements to other approved drugs with and without REMS).

Respondents assert (Opp. 36) that notwithstanding these stringent requirements FDA acted arbitrarily because adverse events were "underincluded" in the data it considered. But the study respondents cite was published in 2021, see D. Ct. Doc. 8

802, and thus was not part of the administrative record when FDA determined that mandatory prescriber reporting of non-fatal adverse events was no longer necessary in 2016. It cannot be arbitrary or capricious for FDA to "fail" to consider evidence that did not exist at the time it made the relevant decision.[7]

c. As to FDA's 2021 and 2023 actions to eliminate the in-person dispensing requirement, the Fifth Circuit faulted the agency for relying on adverse event data that was supposedly tainted by the 2016 reporting changes. Appl. App. 35a. Respondents echo the same argument (Opp. 36). But it is not plausible to assert that mifepristone's post-2016 adverse event reporting regime -- which, again, is more rigorous than the regime applicable to the vast majority of drugs -- cannot be a basis for reasoned decisionmaking. And the Fifth Circuit failed to acknowledge that FDA did not rely on adverse events alone, but also conducted "an extensive review of the published literature." C.A. Add. 864.

Again seeking to plug the gaps in the Fifth Circuit's analysis, respondents criticize (Opp. 37) the "limitations" of some of

[7] There is also good reason to question the impartiality of respondents' study. A co-author of that study (Donna Harrison) is both a declarant in this case and the CEO of respondent American Association of Pro-Life Obstetricians and Gynecologists. D. Ct. Doc. 8 802. The lead author was also affiliated with that respondent, and the third author was employed by the Charlotte Lozier Institute, an amicus supporting respondents in this Court. And the study itself does not identify any meaningful discrepancy between providers' and FDA's data, apart from FDA having a lower number of reports of "ongoing pregnancy." Ongoing pregnancy is typically considered an efficacy (not safety) metric, and thus would not call into question FDA's reliance on its adverse event reports to evaluate mifepristone's safety.

the studies FDA reviewed in determining in 2021 that the REMS should be modified to remove the in-person dispensing requirement. As respondents concede, however, FDA acknowledged those limitations. The agency explained why "[d]espite the limitations of the studies [it] reviewed," those studies (plus other real-world evidence) supported its conclusion that in-person dispensing was no longer necessary. C.A. Add. 864. FDA's detailed evaluation of those studies spans eight pages of its response to respondents' 2019 citizen petition. Id. at 865-872. Respondents do not even discuss this part of the record, let alone explain why FDA's detailed response does not satisfy its obligation to reasonably explain its decisionmaking.

d. The amicus briefs in this case underscore the extent to which the lower courts have strayed from settled principles of administrative review -- and the profoundly destabilizing effects that their mode of analysis would have. A broad coalition of industry participants has warned, for example, that the logic of the lower courts' decisions threatens a "seismic shift in the clinical development and drug approval process," one that would "chill drug development and investment." Amicus Br. of Pharmaceutical Cos. 17-18. And a leading industry organization has likewise warned that the decisions below "strike a severe blow to th[e] settled regulatory framework, and the investments that hinge upon it." Amicus Br. of Pharmaceutical Research and Manufacturers of America 2. In short, the novel approach the lower courts

adopted here threatens to severely disrupt the Nation's critical system for developing, approving, and regulating pharmaceuticals.

2. The Comstock Act Provides No Basis For Invalidating FDA's Decision to Eliminate the In-Person Dispensing Requirement

Respondents briefly assert (Opp. 39-40) that the Comstock Act provides an additional basis for invalidating FDA's elimination of the in-person dispensing requirement. The Fifth Circuit did not endorse that argument, which rests on a misunderstanding of the Comstock Act. See Appl. 41-43; Amicus Br. of Former DOJ Officials 9-21. And in any event, regardless of the Comstock Act's meaning, it would provide no basis to overturn FDA's actions.

The FDCA requires FDA to assess safety and effectiveness when it approves a drug and sets the conditions for its use. See 21 U.S.C. 355(d), 355-1. Nothing in the statute requires FDA to address in those decisions other laws that may restrict the drug's distribution or use. Instead, the FDCA leaves enforcement of those laws to the agencies charged with their administration. For example, the Controlled Substances Act restricts distribution of fentanyl, but FDA has not incorporated those restrictions into its approval or REMS for certain fentanyl products. See Transmucosal Immediate Release Fentanyl Shared System REMS Program (Dec. 2022), https://perma.cc/JK6T-S99C; 21 U.S.C. 841-843.

FDA followed the same practice here. The agency relied on its FDCA authority to require in-person dispensing, but it decided in 2021 that the requirement must be lifted because the evidence

showed that such a requirement was no longer needed to ensure that the benefits of mifepristone outweigh its risks -- and thus that the FDCA no longer justified a prohibition on filling a prescription for mifepristone at a retail pharmacy or by mail. C.A. Add. 863-872. Respondents fail to explain why the Comstock Act required FDA to impose requirements under the FDCA that the FDCA itself no longer supports.

II. THE BALANCE OF HARMS OVERWHELMINGLY FAVORS A STAY

The governmental and public interests overwhelmingly favor a stay. Appl. 38-45. Respondents argue otherwise only by pretending that the Fifth Circuit's order will not have the disruptive consequences that FDA, Danco, and amici have documented.

A. The government's application explained that the Fifth Circuit's order would irreparably harm FDA and the public by upending a settled regulatory scheme: All extant packages of Danco's Mifeprex would be misbranded, and the generic version of the drug would lose its approval altogether. Danco could not lawfully continue to introduce the drug into interstate commerce, see 21 U.S.C. 331(a), 355(a), unless and until FDA and Danco take the steps needed to bring the drug's labeling and conditions of use into alignment with the lower courts' orders -- a "[d]ifficult" process that FDA estimates will take "months." Appl. App. 115a-116a; see Appl. 38-41. It would make little sense to force FDA to make those disruptive changes during the pendency of an expedited appeal only for them to be undone if the district court's order is

ultimately reversed. And it makes even less sense to require FDA to take those steps when doing so would put the agency at risk of violating the injunction issued by the district court in the Washington litigation. See Appl. 41.[8]

Respondents do not attempt to defend that disruption and risk of conflicting court orders. Instead, they pretend it will not occur. On their telling, "[a]ll FDA needs to do is sit tight" and the pre-2016 regulatory regime will spring back to life of its own accord, with no need for any action by FDA and no risk of conflict with the Washington injunction. Opp. 42. But that is demonstrably wrong, as FDA's Principal Deputy Commissioner explained in a declaration detailing the necessary regulatory actions -- including the approval of new labeling and packaging, new prescriber and patient agreements, and the need for most prescribers to become "recertified" and adjust their practice to a different dose and dosing regimen. Appl. App. 110a-116a; see Danco Appl. 32-39. Respondents do not even acknowledge, much less attempt to refute, that showing. And the fact that respondents themselves are unwilling to defend the disruptive effects of the lower courts' orders is reason enough to grant a stay.

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[8] Respondents erroneously assert (Opp. 42) that the government "has not lifted a finger" to avoid the conflict with the Washington injunction. The government opposed that injunction and asked the Washington court for clarification in light of the district court's order in this case. Because the Washington injunction merely requires FDA to maintain the status quo, it does not independently cause irreparable injury -- in contrast to the disruptive lower court orders in this case.

Nor is the irreparable harm limited to the disruption associated with an abrupt return to the pre-2016 regime and the resulting loss of lawful access to mifepristone in the meantime. The lower courts' orders suspend the approval of GenBioPro's generic version of the drug, which the company asserts accounts for two-thirds of the market. Amicus Br. of GenBioPro 2. The pre-2016 conditions of use also impose limits on access that were later shown to be unnecessary, including a requirement that mifepristone be dispensed only in certain medical settings. And those pre-2016 conditions "would also require FDA to reinstate a superseded dosing regimen, requiring a substantially higher dose of the drug than FDA has deemed necessary." Appl. App. 115a.

B. The loss of access to mifepristone caused by the lower courts' orders would impose serious harms. Doctors have explained that mifepristone is used in gynecology for "obstetric care, medication abortion, and miscarriage management," such that limiting availability of mifepristone "will have immediate and far reaching impacts on reproductive health, medical ethics, and patient autonomy." Amicus Br. of Physicians for Reproductive Health 2; see Amicus Br. of Medical and Public Health Societies 18-24. Mifepristone has lawful uses in every State, whether for miscarriage management or otherwise. And millions of women across the country have opted to use mifepristone as an alternative to more-invasive surgical abortion.

Respondents dismiss the harms of requiring women to undergo surgical abortion and denying them access to a drug under conditions FDA determined were safe and effective because those women "are not stay applicants in this case." Opp. 42 (citation omitted). But women who wish to use mifepristone are undoubtedly members of the "public" whose interests must be considered in the stay analysis. See Nken v. Holder, 556 U.S. 418, 434-435 (2009). They are also the patients whose interests the FDCA approval process is designed to further. Respondents assert (Opp. 47-48) that the lower courts' orders will actually protect women who might otherwise suffer adverse effects from mifepristone. But that argument ignores the agency of the affected women, who are in the best position to decide what is in their interests. FDA's conditions of use allow mifepristone to be dispensed only after a woman has consulted with her health care provider and been informed about the drug's risks. The lower courts' orders interfere with women's ability to make that intensely personal medical decision for themselves.

C. Respondents' own purported harms pale in comparison, and certainly do not justify the deep disruption that will occur absent a stay. Respondents' central contention is that if mifepristone were available under the pre-2016 conditions rather than the 2023 conditions, the risk that their members would be called upon to treat an (exceedingly rare) serious adverse event in the future would be reduced. Even if that attenuated, probabilistic injury

could satisfy Article III, it would not justify preliminary relief. No emergency justified the lower courts' decision at a preliminary stage of this APA suit to grant abrupt and sweeping relief that fundamentally altered the status quo prior to full merits resolution, instead of allowing this litigation to play out in the ordinary course.

Respondents' own conduct underscores the point. Respondents delayed for years before petitioning FDA to reconsider the modifications made in 2016, waited nearly a year to challenge the denial of that 2019 petition, and then disclaimed a need for preliminary relief and instead asked the district court to consolidate their preliminary injunction motion with a full trial on the merits. That history belies any need for immediate relief, or any equitable basis for respondents to be granted such relief. Respondents invoke (Opp. 45) the FDA's delay in adjudicating their 2002 citizen petition. But that is a non sequitur. The 2002 citizen petition is not at issue here because the Fifth Circuit concluded that respondents failed to timely challenge FDA's decision denying it. And the agency's delay in connection with a different petition in no way diminishes the relevant point: Respondents' own conduct during this litigation further confirms that they would not be irreparably harmed by the maintenance of the status quo while this case proceeds. There is thus no justification for the extraordinarily disruptive nationwide preliminary relief granted below. This Court should preserve the status quo

by staying in full the district court's erroneous and inequitable order.

CONCLUSION

The application for a stay pending proceedings in the Fifth Circuit and (if necessary) further proceedings in this Court should be granted. If the Court does not rule before the existing administrative stay expires at 11:59 p.m. tomorrow evening, it should extend that stay pending the resolution of this application.

Respectfully submitted.

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